

Amendments to the Specification:

Please replace the following paragraphs with the revised versions provided herein below:

Bridging pages 32 and 33, beginning at line 29 on page 32 through line 22 on page 33:

"HIM2 may be synthesized by various methods as will be understood by those skilled in the art. HIM2 is preferably synthesized utilizing proinsulin as a starting material as described in U.S. Patent Application Serial No. 10/036,744 filed December 21, 2001 by Soltero et al. entitled "Methods of Synthesizing Insulin Polypeptide-Oligomer Conjugates, and Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same." For example, HIM2 has been synthesized as follows. Recombinant proinsulin having a leader peptide (MW 10,642 Daltons) was obtained from Biobras, of Belo Horizonte, Brazil. A 2.32×10^{-3} mmol portion of the proinsulin was dissolved in 10 mL of DMSO. To the solution was added 324 μ L of triethylamine. The resulting solution was allowed to stir for 5 minutes, and then a solution of activated methylheptaethylene glycol ((PEG7)-hexyl oligomer) (9.30×10^{-3} mmol) in acetonitrile was added. The course of the conjugation (acylation) reaction was monitored by HPLC. When reaction appeared to be complete, it was quenched by addition of 3.54 mL of 5% aqueous trifluoroacetic acid solution. The reaction mixture was then processed and exchanged into 100 mM Tris-HCl Buffer, pH 7.6 to provide a product mixture. An aliquot of the Tris-HCl solution of the product mixture was analyzed by HPLC to determine the polypeptide concentration. A solution of trypsin (TPCK treated; from bovine pancreas) was prepared in 100 mM Tris-HCl Buffer, pH 7.6. A solution of carboxypeptidase B (from porcine pancreas) was prepared in 100 mM Tris-HCl Buffer, pH 7.6. The product mixture (0.424 μ mol/mL) was then allowed to react with trypsin (5.97×10^{-4} μ mol/mL) and carboxypeptidase B (1.93×10^{-4} μ mol/mL). After 30 minutes, the reaction was quenched by the addition of 1.58 mL of 1% trifluoroacetic acid in acetonitrile. The major products were identified by HPLC retention time (relative to the retention times of known reference standards) and mass spectral analysis. Insulin (10%) and Lys^{B29}-Hexyl-PEG7-Oligomer-Conjugated Insulin (84%) were thus obtained."

Bridging pages 33 and 34, beginning at line 29 on page 33 through line 19 on page 34:

"The insulin polypeptide-oligomer conjugates employed in the various embodiments described above may be synthesized by various methods as will be understood by those skilled in the art. For example, polydispersed insulin polypeptide-oligomer conjugates may be synthesized by the methods provided in one or more of the following references: U.S. Patent No. 5,359,030 to Ekwuribe; U.S. Patent No.

5,438,040 to Ekwuribe; U.S. Patent No. 5,681,811 to Ekwuribe; U.S. Patent No. 6,309,633 to Ekwuribe et al.; and U.S. Patent Application Serial No. 10/036,744 filed December 21, 2001 by Soltero et al. entitled "Methods of Synthesizing Insulin Polypeptide-Oligomer Conjugates, and Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same", the disclosures of which are incorporated herein by reference in their entireties. Non-polydispersed (e.g., substantially monodispersed and monodispersed) insulin polypeptide-oligomer conjugates may be synthesized by methods provided in one or more of the following references: U.S. Patent Application Serial No. 09/873,797 filed June 4, 2001 by Ekwuribe et al. entitled "Mixtures of Drug-Oligomer Conjugates Comprising Polyalkylene Glycol, Uses Thereof, and Methods of Making Same"; U.S. Patent Application Serial No. 09/873,899 filed June 4, 2001 by Ekwuribe et al. entitled "Mixtures of Insulin Drug-Oligomer Conjugates Comprising Polyalkylene Glycol, Uses Thereof, and Methods of Making Same"; U.S. Patent Application Serial No. 10/036,744 filed December 21, 2001 by Soltero et al. entitled "Methods of Synthesizing Insulin Polypeptide-Oligomer Conjugates, and Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same", the disclosures of which are incorporated herein by reference in their entireties. Oligomers according to embodiments of the present invention are preferably substantially monodispersed and are more preferably monodispersed."